

Why was there no Vaccine-associated Intussusception in Indian Rotavirus Vaccine Trial?

Recently, two papers have been published on the phase 3 efficacy trial of the Indian rotavirus vaccine (Rotavac) [1,2]. The study sites were Delhi (urban), Pune (rural) and Vellore (urban and rural) [1,2]. A total of 4532 infants were assigned to vaccine group and 2267 to placebo group in this randomized, double-blind, placebo controlled study [1,2]. Vaccine efficacy (VE) against severe rotavirus gastroenteritis was 53.6 percent in the first year and 48.9 percent during the second year after vaccination [1,2]. These results are comparable to VE of the other licensed rotavirus vaccines in tropical developing countries [1,2].

Rotavirus vaccine-associated intussusception is expected to occur within 7 to 14 or maximum 30 days after any dose in the schedule. Among the 4500 infants given 3 doses of Rotavac, none developed intussusception after dose 1 or 2 and during 100 days (>3 months) after third dose [1]. Although there was no vaccine-associated intussusception in this study, we cannot extrapolate to suggest *carte blanche* that Rotavac does not trigger intussusception.

Why was there no intussusception associated with Rotavac in the study? There are three possible explanations for this salutary safety record. First, the schedule was with three doses given at 6, 10 and 14 weeks. This is the age with comparatively lower frequency of spontaneous intussusception [3]. The prevalence begins to rise from 20 weeks of age, which would be 5-6 weeks after the third dose [3]. Second, the Indian rotavirus vaccine is derived from a naturally

occurring strain of human (neonatal nursery) rotavirus, unlike other vaccines that are either bovine origin virus or laboratory manipulated strains [1]. It is possible that the neonatal human strain is less prone to trigger intussusception than other vaccine strains in use; this needs to be explored in a larger study and in post-marketing surveillance. Third, the risk of vaccine-associated intussusception is very small; such a rare event may not have occurred in the sample size of 4,500, purely due to chance.

In summary, the absence of vaccine-associated intussusception in the vaccine trial is not to be taken as proof that Rotavac will not trigger it when given to very large numbers of infants. However, it gives the Government confidence that Rotavac is suitable for inclusion in the Universal Immunization Programme (UIP). If and when the Indian rotavirus vaccine is included in UIP, post-marketing surveillance must be established to measure the risk of vaccine-associated intussusception, particularly in infants given any dose beyond 14 weeks of age.

T JACOB JOHN

*President, Child Health Foundation, India.
tjacobjohn@yahoo.co.in*

REFERENCES

1. Bhandari N, Rongsen-Chandola T, Bavdekar A, Jacob J, Antony K, Taneja S, *et al.* Efficacy of a monovalent human-bovine (116E) rotavirus vaccine in Indian infants: a randomized, double-blind, placebo-controlled trial. *Lancet*. 2014;383:2136-43.
2. Bhandari N, Rongsen-Chandola, Bavdekar A, Jacob J, Antony K, Taneja S, *et al.* Efficacy of a monovalent human-bovine (116E) rotavirus vaccine in Indian children in the second year of life. *Vaccine*. 2014; 32:A110-6.
3. Jehangir S, John J, Rajkumar S, Mani B, Srinivasan R, Kang G. Intussusception in southern India: comparison of retrospective analysis and active surveillance. *Vaccine* 2014; 32(Suppl.1): A99-103.

The Dilemma of Reactive NS1 Antigen Test in Dengue Fever

Dengue NS1 antigen test assays are very useful in the diagnosis of dengue fever with good sensitivity and specificity during the first week of illness [1]. There has been wide spread use of Dengue ELISA NS1 antigen test. In an outbreak setting, NS1 antigen may not necessarily be

an indicator for severe dengue infection or of need for hospitalization. Since 2012, Puducherry has experienced an unprecedented rise in dengue fever cases. We confirmed the diagnosis of dengue fever either by ELISA-based NS1 antigen test or dengue serology for IgM and IgG antibodies. Among 261 diagnosed cases of Dengue fever, NS1 antigen was positive in 217 cases (56.4%); 44 cases (31.4%) were negative for NS1 antigen assay and positive for IgM MAC ELISA. Among the children who were positive only for NS1 antigen, non-severe dengue infection was the most common mode of presentation.